Please amend the subject application as follows:

In the Claims:

Please amend the claims as follows.

Please cancel claims 105-116 without prejudice or disclaimer.

REMARKS

Claims 98-116 are pending in the application. Claims 105-116 have been cancelled without prejudice or disclaimer of applicants' right to pursue the subject matter of one or more of these claims in a subsequent application. Entry of this Amendment is therefore respectfully requested such that claims 98-104 will be pending in the application.

Allowable Subject Matter

Applicants note with appreciation the Examiner's statement at page 6 of the Office Action that applicant[s] has rewritten claim 99 in independent form and that [the claim] is allowable.

The Examiner additionally stated that claim 110 is not anticipated by Wu et al. because the epitope of PA14 is D2 in the N-terminus and R168 [of] in ECL2, citing to the specification at page 38, lines 11-13. The Examiner stated that, although Wu et al. anticipates an antibody that binds to the N-terminus and ECL2 of CCR5, the reference does not teach that the antibody binds to these specific amino acid sequences.

The Examiner also stated that on page 17 of the response [i.e., Paper No 12 filed September 18, 2002], applicant stated that page 10 of the Office Action indicated that antibodies having a specificity to a conformational epitope that comprises the N-

terminus and the second extracellular loop of CCR5 are not taught or suggested by the prior art. The Examiner stated that this statement is incorrect, as evidenced by the teachings of Wu et al. cited on page 6 of the previous rejection and in the instant rejection under 35 U.S.C. §102. The Examiner stated that the indicated allowable subject matter is drawn to the specific antibodies recited in originally presented claim 98.

Applicants maintain the antibody embraced by claim 110 is monoclonal and monospecific for a single conformational epitope. It is not a bispecific antibody having specificity for multiple epitopes as disclosed in Wu et al.

Claim Objections

The Examiner stated on page 2 of the Office Action that claim 105 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not depend from another multiple dependent claim, citing to MPEP §608.01(n). The Examiner stated that accordingly, claim 105 has not been further treated on the merits.

In response, applicants have canceled claim 105 without prejudice or disclaimer to their right to pursue patent protection for the subject matter of this claim in a subsequent application. The cancellation of claim 105 renders the Examiner's objection to this claim moot.

Double Patenting Rejection

On page 2 of the Office Action, claims 98, 100-104 and 106-116 are provisionally rejected under the judicially-created doctrine of double patenting over claims 70-80 of copending Application No. 09/464,902 [the '902 application] for the reasons of record.

The Examiner stated that this is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The Examiner stated that applicant[s] traverses the rejection on the grounds that the antibodies are not being examined in the '902 application due to an election of a group drawn to nucleic acids. The Examiner further stated that applicants arguments have been fully considered, but are found unpersuasive because there is no record of an election in the '902 application.

In response, the Examiner's attention is respectfully directed to pages 7-13 of their Amendment In Response To September 25, 2001 Office Action And Petition For a Five Month Extension of Time which was filed March 29, 2002 in application Serial No. 09/464,902 in response to a Requirement for Election issued in the subject '902 application. In particular, in the paragraph bridging pages 9-10 of the Amendment, Applicants elected with traverse to prosecute the claims of the Examiner's Group VI, nos. 87-88, drawn to nucleic acids encoding CDR regions of an anti-CCR5 monoclonal antibody. Additionally, in response to a further election requirement issued by the Examiner of the subject application (Examiner Robert D. Budens, Art Unit 1648) applicants elected nucleic acids reading on murine monoclonal antibodies. Applicants have, in their file, a return post card, stamped by the Office, as evidence of the Office's receipt of their Amendment containing the above-described election on March 29, 2002.

Notwithstanding the above, the Examiner of this application stated on page 3 of the present Office Action that even if the election were of record, claims to the monoclonal antibodies are still pending in both applications. The Examiner then further

stated that, to obviate this rejection, it is suggested that applicant[s] cancel the monoclonal antibody claims in the '902 application, i.e., claims 78-80.

The cancellation of claims 105-116, without prejudice or disclaimer renders the double patenting rejection of claims 106-116 moot. As to the provisional double-patenting rejection of claims 98 and 100-104 over claims 78-80 of Application No. 09/464,902, applicants submit that the rejection is respectfully traversed. Applicants submit that M.P.E.P. §804 IB, in discussing provisional double-patenting rejections between copending applications, requires that the:

> 'provisional' double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that provisional double patenting rejection is the only rejection remaining in one of the applications. If the 'provisional' double patenting rejection in one application is the only rejection remaining in the application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the 'provisional' double patenting rejection in the other application into a double patenting rejection at the time one application issues as a patent. (emphasis supplied by applicants).

Claims 98-104 are pending in this application in view of the cancellation, without prejudice or disclaimer, of claims 105-116.

Claim 99 has already been allowed by the Examiner. The only remaining ground for rejection of claims 98 and 100-104 is the provisional double patenting rejection. In accordance with the M.P.E.P. section quoted above, the provisional double patenting rejection should therefore be withdrawn to permit claims 98-104 to issue as a patent. Such action is therefore respectfully solicited.

Rejections Under 35 USC §112

Claim 106 and claims 109-115, which depend directly or indirectly on claim 106, are rejected on page 3 of the Office Action under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant[s] regards as the invention. The Examiner stated that claim 106 is drawn to a monoclonal antibody or a fragment thereof that specifically binds to an epitope on CCR5. The Examiner stated that the claim states that the epitope comprises two amino acid sequences and that one such sequence is a "portion" of an amino terminal region while the second sequence comprises a "portion" of an extracellular loop region 2 (ECL2). The Examiner stated that the metes and bounds of the "portions" recited in the claims are vague and indefinite. The Examiner additionally stated that section (b) of the claim recites, "at a defined concentration" but does not recite what the concentration is. The Examiner also stated that it cannot be determined what the, "same defined concentration" is in section (c). The Examiner further stated that this rejection [also] affects claims 109-115.

In response, applicants submit that the cancellation of claims 105-116 from this application, without prejudice or disclaimer, renders this rejection moot.

Rejections Under 35 USC §102

Claims 106, 109, 111, 112 and 114-116 are rejected under 35 U.S.C. §102(a) on page 4 of the Office Action as allegedly being anticipated by Wu et al. (WO 98/18826). The Examiner stated that claim 116 is drawn to a monoclonal antibody comprising a single set of light and heavy chain CDRs that bind to an epitope located in the N-terminus and one of the three extracellular loops of CCR5. The Examiner stated that claim 106 is drawn to a monoclonal antibody or a fragment that specifically binds to an epitope on CCR5 that comprises at least two amino acid sequences. The Examiner stated that the first sequence comprises a portion of the N-terminal region of CCR5 and the second sequence comprises a portion of the ECL2. The Examiner stated that this antibody inhibits HIV-1 infection of a CD4+ CCR5+ cell and does not antagonize the activity of CCR5 in response to certain chemokines listed in claim 109.

The Examiner then went on to state that Wu et al. teaches a bispecific antibody that binds to the N-terminus and the second extracellular loop of CCR5, citing to the text of the reference from page 15, line 27 to page 16, line 5. The Examiner stated that this antibody clearly anticipates claims 116 and 106. The Examiner stated that Wu et al. teaches that this antibody inhibits HIV infection of a cell, citing to claim 12, and inhibits the interaction between CCR5 and one or more of its ligands, such as RANTES, MIP-1α and MIP-1β, citing to page 19, lines 11-14 and claims 5, 30 and 31.

The Examiner stated that claims 111 and 112 are drawn to the antibody comprising a human immunoglobulin molecule. The Examiner further stated that Wu et al. teaches humanized forms of the antibodies, where the framework and the consensus are derived from a human immunoglobulin or multiple immunoglobulin molecules,

citing to page 19, line 31 to page 21, line 32.

The Examiner additionally stated that claims 114 and 115 are drawn to the antibody labeled with a detectable marker. The Examiner stated that Wu et al. teach a method of detecting the expression of CCR5 on a cell by detecting the binding of the antibody to the cell (citing to claim 16 as an example). The Examiner stated that although Wu et al. does not explicitly teach that the antibody is labeled, the antibody of claim 16 [sic. 116] would have to possess a label for its presence to be detected. The Examiner stated that Wu et al. also teaches identifying an agent with a fluorescent or radioactively labeled antibody, citing to claims 62 and 64.

The Examiner stated that applicant[s] argues that the bispecific antibodies of Wu et al. recognize at least two different epitopes and that the antibody of Wu et al. does not anticipate the instant invention. The Examiner stated that applicant[s] asserts that the claimed antibody is monospecific and recognizes one non-contiguous epitope on CCR5.

The Examiner stated that applicants' arguments have been fully considered but have been found unpersuasive. The Examiner stated that the claims are drawn to a monoclonal antibody that binds to an epitope comprising the N-terminus and ECL2. The Examiner stated that the instant antibody is bi-specific for two different amino acid sequences in different regions of the CCR5 molecule. The Examiner stated that the antibody of Wu et al. is also bi-specific for the N-terminus and ECL2 and recognizes the identical epitope recited in the claims.

In response, applicants submit that the cancellation of claims 105-116 from this application, without prejudice or disclaimer,

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renders this rejection moot.

Applicants again reiterate that the monoclonal antibodies of the present invention are monospecific, are directed to a single conformational epitope on CCR5 and are not bispecific antibodies as taught by Wu et al having specificity for multiple epitopes on CCR5.

Rejections Under 35 USC §103

Claim 113 is rejected under 35 U.S.C. 103(a) on page 5 of the Office Action as being allegedly unpatentable over Wu et al. *supra*. The Examiner stated that the claim is drawn to specific human immunoglobulin molecules, such as IgG1.

The Examiner stated that applicants should see the teachings of Wu et al. The Examiner stated that the reference does not teach the specific immunoglobulins listed in the claims, however Wu et al. teaches antibodies in humanized form where the framework is derived from a human immunoglobulin. The Examiner stated that, therefore, any specific human immunoglobulin would be an obvious choice to the ordinary artisan.

In response, applicants submit that the cancellation of claims 105-116 from this application, without prejudice or disclaimer, renders this rejection moot.

Applicants submit that even in a humanized form as recited in claim 113, the antibody of the present invention is monospecific, is directed to a single conformational epitope on CCR5 and is not rendered obvious in view of Wu et al that teaches bispecific antibodies having specificity for multiple epitopes on CCR5.

Supplemental Information Disclosure Statement

In compliance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references, which are listed on the accompanying form PTO-1449 (**Exhibit A**), copies of which are attached hereto as **Exhibits B-K.**

1. Wu, et al., U.S. Patent No. 6,528,625, issued March 4, 2003, filed July 11, 1997. (Exhibit B).
2. Li, et al., U.S. Patent Application Publication No. US 2003/0023044, published January 30, 2003, filed September 3, 2002. (Exhibit C).
3. Rosen, et al., U.S. Patent Application Publication No. US 2002/0048786, published April 25, 2002, filed February 9, 2001. (Exhibit D).
4. Rosen, et al., U.S. Patent Application Publication No. US 2002/0061834, published May 23, 2002, filed February 9, 2001. (Exhibit E).
5. Li, et al., U.S. Patent Application Publication No. US 2002/0076745, published June 20, 2002, filed November 18, 1998. (Exhibit F).
6. Li, et al., U.S. Patent Application Publication No. US 2002/0099176, published July 25, 2002, filed June 25, 1999. (Exhibit G).
7. Samson, et al., U.S. Patent Application Publication No. US 2002/0106742, published August 8, 2002, filed August 24, 2001. (Exhibit H).
8. Samson, et al., U.S. Patent Application Publication No. US 2002/0110805, published August 15, 2002, filed August 24, 2001. (Exhibit I).
9. Samson et al., U.S. Patent Application Publication No. US 2002/0110870, published August 15, 2002, filed August 24, 2001. (Exhibit J).

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10. Li, et al., U.S. Patent Application Publication No. US 2002/0132269, published September 19, 2002, filed February 11, 2000. (Exhibit K).

None of the above references are believed to teach or suggest the presently claimed invention, whether taken alone or in combination with any other cited reference(s).

The undersigned hereby certifies, under 37 C.F.R. 1.98 (e)(2), that no item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in §1.56(c) more than three months prior to the filing of the information disclosure statement.

The Examiner is respectfully requested to make the references cited above of record in the present case by initialing and dating a copy of the form PTO-1449 attached hereto as Exhibit A and returning it to applicants' representative with the next communication concerning this application.

A fee of ONE HUNDRED EIGHTY DOLLARS ($180.00) is believed due under 37 C.F.T. §1.17(p) for submission of this Supplemental Information Disclosure Statement. A check including the amount of this fee is enclosed herewith.

Summary

For all of the reasons set forth above, therefore, claims 98-104 are believed to be in condition for allowance. The Examiner is respectfully requested to reconsider and withdraw all of her

objections and rejections as they concern the subject claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

A total fee of $645.00, including a $465.00 fee for a three month extension of time and a $180.00 fee for submission of a Supplemental Information Disclosure Statement ($465.00 +$180.00 =$645.00) is believed to be due with this Amendment. However, if any additional fee is required, authorization is hereby provided to charge the required fee to Deposit Account No. 03-3125. As noted above, a separate Notice of Appeal concerning this application is being filed on the same day as this Amendment. The Notice of Appeal is timely filed on account of the Petition for a three-month extension submitted with this Amendment. The fee due with the Notice of Appeal is being separately submitted with the Notice.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, V.A. 22313-1450

Mark A. Farley 6/3/03

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